

CLAIMS

5 1. Diagnostic agent comprising a compound of formula :

(PEPTIDE) n_1 – (LINKER) n_2 – (SIGNAL) n_3 (I)

wherein

1) PEPTIDE is chosen in the group :

a) $X_1 - X_2 - X_3 - X_4 - NHOH$ (II),

10 wherein

X_1 is absent or X_1 is a residue of an alpha-amino glycine, X_2 is a residue of an amino acid selected from proline, hydroxyproline, thioproline and alanine, X_3 is a residue of an amino acid selected from glutamine, glutamic acid, leucine, isoleucine and phenylalanine and X_4 is a residue of an alpha-amino acid selected from glycine, alanine, valine, leucine ;

15 and the hydrogen atom of the amino group in said alpha-amino acid X_1 may be replaced with a member X_0 selected from the group consisting of acetyl, benzoyl (Bz), benzyloxy, t-butyloxycarbonyl, benzyloxycarbonyl (Z), p-aminobenzoyl (ABz), p-amino-benzyl, p-hydroxybenzoyl (HBz), 3-p-hydroxyphenylpropionyl (HPP).

b) a peptide functionally equivalent to a peptide of a)

c) a peptidic fragment of (II) functionally equivalent to a peptide of a) or b)

25 2) SIGNAL is a signal entity for medical imaging

3) LINKER eventually absent represents a chemical link between PEPTIDE and SIGNAL

; and the pharmaceutical salts thereof.

30 2. Diagnostic agent of claim 1 wherein X_1 is absent or X_1 is glycine, X_2 is a residue of an amino acid selected from proline, hydroxyproline,

thioproline, X3 is a residue of an amino acid selected from leucine, isoleucine and phenylalanine and X4 is a residue of an alpha-amino acid selected from glycine, alanine.

- 5 3. Diagnostic agent of claim 1 wherein PEPTIDE is X-NHOH with X chosen among : Abz-Gly-Pro-D-Leu-D-Ala, HBz-Gly-Pro-D-Leu-D-Ala, Abz-Gly-Pro-Leu-Ala, Bz-Gly-Pro-D-Leu-D-Ala, Bz-Gly-Pro-Leu-Ala, HPP-Pro-D-Leu-D-Ala, HPP-Pro-Leu-Ala, Z-Pro-D-Leu-D-Ala, Z-Pro-Leu-Ala.
- 10 4. Diagnostic agent of claim 1 to 3 wherein PEPTIDE is p-aminobenzoyl-Gly-Pro-D-Leu-D-Ala-NHOH.
5. Diagnostic agent of claim 1 to 4 wherein SIGNAL is macrocyclic or linear chelate chosen among DTPA, DOTA, DTPA BMA, BOPTA, DO3A, HPDO3A, TETA, TRITA, HETA, M4DOTA, DOTMA, MCTA, PCTA and the derivatives thereof.
- 15 6. Diagnostic agent of claim 1 to 4 wherein SIGNAL is a lipidic nanoparticule, a liposome, a nanocapsule wherein the SIGNAL is a carrier of a diagnostic metal chelate.
- 20 7. Diagnostic agent of claim 1 to 6 wherein said agent is coupled to a metal element M chosen among an ion of a paramagnetic metal of atomic number 21-29, 42-44, or 58-70, namely Gd, or a radionuclide, typically ⁹⁹Tc, ¹¹⁷Sn, ¹¹¹In, ⁹⁷Ru, ⁶⁷Ga, ⁶⁸Ga, ⁸⁹Zr, ¹⁷⁷Lu, ⁴⁷Sc, ¹⁰⁵Rh; ¹⁸⁸Re, ⁶⁰Cu, ⁶²Cu, ⁶⁴Cu, ⁶⁷Cu, ⁹⁰Y, ¹⁵⁹Gd, ¹⁴⁹Pr, ¹⁶⁶Ho.
8. Diagnostic agent of claim 1 to 4 wherein SIGNAL is an iron oxide particle.
- 25 9. Diagnostic agent of claim 8 wherein the particle is coated with a gem-bisphosphonate.
10. Use of a compound of claim 9 for the diagnostic of a cardiovascular/atheroma disease.
11. Use of compound of claim 1 to 9 for the preparation of an agent for the diagnostic of a cardiovascular/atheroma disease.
- 30

12. Method of preparation of a compound of claim 1 to 8 comprising the coupling of a peptide X1 -X2 -X3 -X4-NHOH and a SIGNAL entity.

5 13 Method of detecting, imaging or monitoring the presence of matrix metalloproteinase in a patient comprising the steps of: a) administering to said patient a diagnostic agent of claim 1 to 9 ; and b) acquiring an image of a site of concentration of said diagnostic agent in the patient by a diagnostic imaging technique.

10 14 Method of detecting, imaging or monitoring a pathological disorder associated with matrix metalloproteinase activity in a patient comprising the steps of: a) administering to said patient a diagnostic agent according to claim 1 to 9 ; and c) acquiring an image of a site of concentration of said diagnostic agent in the patient by a diagnostic imaging technique.

15 15. Method according to claim 14, wherein the atherosclerosis is coronary atherosclerosis or cerebrovascular atherosclerosis.

20 16. Method of identifying a patient at high risk for transient cerebral ischemic attacks or stroke by determining the degree of active atherosclerosis in a patient comprising carrying out the method of claim 15.

25 17 Method of identifying a patient at high risk for acute cardiac ischemia, myocardial infarction or cardiac death by determining the degree of active atherosclerosis by imaging the patient by the method of claim 15.